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Case Report

First case of *Tsukamurella pulmonis* infection in an immunocompetent patient

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We report a case of pneumonia due to *Tsukamurella pulmonis* in a 76-year-old immunocompetent woman with chronic pulmonary disease. Microbiological diagnosis was made by bacteriological and molecular means and infection was cured by empirical antibiotic treatment. This work highlights the potential role of *Tsukamurella* in pathogenesis of pneumonia in immunocompetent patients.

1. Case report

A 76-year-old woman with chronic respiratory failure in chronic obstructive pulmonary disease (COPD) arrived at the accident and emergency department with a 2-day history of altered state of consciousness and increasing dyspnoea.

Her medical history included: long history of use of tobacco (34.5 pks/yr), domiciliary oxygen therapy, obesity, diabetes mellitus well-controlled by oral hypoglycaemic drugs, systemic arterial hypertension, bilateral glaucoma, left nephrectomy for kidney stone complicated by acute renal failure, without history of immunodeficits and allografts.

The first examination revealed that the patient was apyretic, dyspnoeic, tachypnoeic, with a blood pressure of 130/70 mmHg, and respiratory rate of 38 breaths per min. The patient appeared confused, responsive to painful stimuli. On auscultation lower pulmonary fields were ipophonetic and vescicular murmur was reduced bibasaly. Laboratory examinations, chest radiograph (CXR) and blood gas analysis (BGA) were performed. BGA results were: FiO_2: 0.50, paO_2: 129 mmHg, pCO_2: 110 mmHg, pH: 7.24. CXR showed: large patchy areas of bilateral alveolar involvement with ground-glass like features in the anterior segment of right upper lobe. Paracardiac parenchyma of right lower lobe, lower two-thirds of the left lung parenchyma, lingula (*silhouette sign*) and lower left lobe (*air-bronchogram sign*) showed alveolar involvement with both ground-glass and consolidation like features. Moreover, small bilateral effusion and radiographic signs of COPD were present (Fig. 1A).

In Intensive Care Unit (ICU), the patient underwent a trial of non-invasive mechanical ventilation without benefit and thereafter the patient underwent oro-tracheal intubation and was mechanically ventilated for 3 days. She was started on empirical antibiotic treatment with amoxicillin–clavulanic acid and azithromycin immediately after bronchoalveolar lavage (BAL) cultures.

The general clinical improvement allowed the transfer to the department of Pulmonary Medicine. At arrival the patient was eupnoic, had productive cough and bilateral leg oedema. BGA results were: FiO_2: 0.31, paO_2: 71.4 mmHg, pCO_2: 63.3 mmHg, pH: 7.36, $HCO3^-$: 31.8 mmol/L, BE: 8.2 mmol/L. She underwent a new trial of non-invasive ventilation (mode: pressure support, inspiratory positive airway pressure: 16 cmH_2O, espiratory positive airway pressure: 6 cmH_2O, target volume: 350 mL, and with supplemental oxygen of 2 litres per min.), with good compliance and

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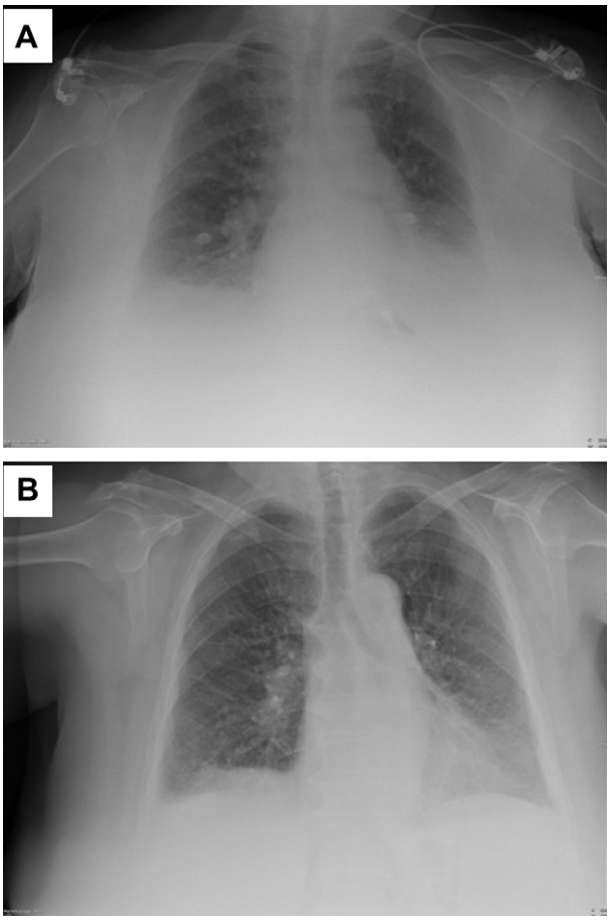

Fig. 1.

improvement of blood gas values. Cultures of BAL, performed immediately after hospital admission in ICU, yielded *Staphylococcus epidermidis* sensitive to ciprofloxacin. Cultures of sputum sample, performed within 48 hours after the transfer to the department of Pulmonary Medicine, yielded *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*, both sensitive to ciprofloxacin and levofloxacin. Then, antibiogram-guided therapy was started: azithromicin was replaced with ciprofloxacin, while amoxicillin–clavulanic acid was continued. Both BAL and sputum sample were processed for isolation of mycobacteria following standard procedures.[7] After 1 week it was observed a general clinical improvement: BGA results were: FiO_2: 0.28, paO_2: 69.8 mmHg, pCO_2: 53.8 mmHg, pH: 7.39, HCO_3^-: 30.3 mmol/L, and BE: 6.6 mmol/L. However, CXR still showed: reduced bilateral pleural effusion with residual basal ipoventilation. Both cultures from BAL and the sputum sample, processed for isolation of mycobacteria, yielded a positive culture in MGIT 960 (Becton Dickinson) and in Lowenstein–Jensen. The strain isolated in culture was subjected to Ziehl–Nielsen staining, showing a weak acid–alcohol-fast staining and a rod shape. Subculture was observed in Trypticase Soy agar, Middlebrook 7H11 agar, nutrient agar, and MacConkey agar without crystal violet, with an abundant growth in the first 48 hours. Colonies were not-pigmented (white-cream) and ranged in size from 2 to 5 mm in diameter (Fig. 2). The microorganism grew at 28 and 35 °C but not at 42 °C. Based on these observation there were strong indication for an atypical, rapidly growing, *Mycobacterium* spp., but no mycobacteria were identified. A negative result with the Quantiferon Test excluded an infection by

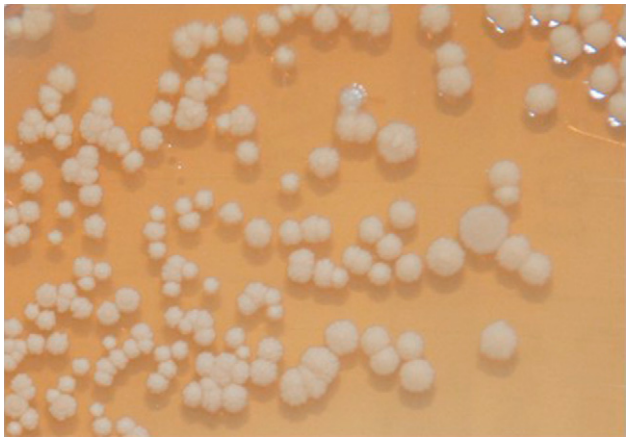

Fig. 2.

M. tuberculosis. To properly identify the microorganism, genomic DNA was extracted from the isolate with the Qiagen EZ1 tissue kit, following the manufacturer's instructions, and the 16S RNA DNA was amplified by PCR and subjected to automated gene sequencing.[3,6] The results obtained identified the microorganism as *T. pulmonis*. Biochemical tests such as semi-quantitative catalase and 68 °C heat-stable catalase confirmed the molecular results and the phenotypic identification using the API Coryne system, RapID CB Plus system and API 20 C AUX system led to the biochemical identification with the numerical profile of, 2150004, 0627511, 6042160, respectively.

Drug susceptibility test was performed by E-test diffusion agar method (AB BIODISK, Solna, Sweden), yielding the following MICs: VAN 4 μg/ml; IPM >32 μg/ml; CLR 2 μg/ml; LVX 0.35 μg/ml; PEN >4 μg/ml; AMC >32 μg/ml; ERY 2 μg/ml; TET 2 μg/ml and CIP 0,25 μg/ml.

The patient was discharged and continued ciprofloxacin for 10 days and after 2 months, she performed a follow-up visit at our Ambulatory of Respiratory Medicine: physical examination revealed that the patient was apyretic, eupnoeic, respiratory rate of 24 breaths per min, and chest examination was normal; BGA results were: FiO_2: 0.21, paO_2: 69.4 mmHg, pCO_2: 43.6 mmHg, pH: 7.40. CXR showed: complete resolution of alveolar and pleural involvement (Fig. 1B).

2. Discussion

The genus *Tsukamurella* was first described by Collins et al. in 1988 following the reclassification and further molecular and phenotypic characterization of *Gordiana aurantiaca*, *Rhodococcus aurantiaca* and other related organisms including *Corynebacterium paurometabola*, which were distinct from the other mycolic acid-containig actinomycetes.[4]

The genus is phylogenetically related to the genera *Nocardia*, *Gordonia*, *Streptomyces*, *Rhodococcus*, *Corynebacterium* and *Mycobacterium* and taxonomically comprises of at least eight described species including *T. inchonensis*, *T. paurometabola*, *T. pseudospumae*, *T. pulmonis*, *T. spumae*, *T. strandjordii*, *T. tyrosinosolvens* and *T. wratislaviensis*.[2]

Tsukamurella is a Gram-positive, variable rod-shaped, weakly acid–alcohol-fast, non-motile, aerobic bacterium. It has been reported as a cause of infections in humans with immunosuppression and indwelling foreign bodies. It has also been isolated in one patient with AIDS (Acquired Immunodeficiency Syndrome) as a saprophytic organism.

Microbiological diagnosis of *Tsukamurella* sp. is cumbersome,[1,5,9] due mostly to the similarity of *Tsukamurella* to other more

common pathogens that are usually isolated in immunocompromised patients, such as Mycobacteria. The implementation of molecular identification by sequencing of the 16S rRNA gene may be particularly useful and may lead to a correct diagnosis in a short time frame.

Tsukamurella infections have emerged over the last decade as a rare but significant cause of serious infection in immunocompromised patient.[8] Moreover there has been a report of the colonization of a patient with *T. pulmonis* subsequent to a *M. tuberculosis* infection.[10]

In our case, lung infection could not be attributed to either *P. aeruginosa* or to *S. maltophilia* because they were not present in BAL performed at admission in ICU. Therefore, the detection of these bacteria outlines nosocomial infection. Finally, the detection of *T. pulmonis* and *S. epidermidis* on BAL sample makes the first bacterium responsible for the lung infection, although both are susceptible to the same antibiotic.

To our knowledge, this is the first case of respiratory infection from *T. pulmonis* in an immunocompetent patient, at risk as diabetic.

Conflict of interest statement

None of the authors have a conflict of interest to declare in relation to this work.

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